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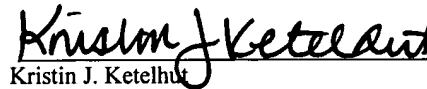
DOCKET NO.: I0248.70024US00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Adams et al.  
Serial No.: 10/616,409  
Confirmation No.: 9289  
Filed: July 9, 2003  
For: BOROPROLINE COMPOUND COMBINATION THERAPY  
Examiner: Not Yet Assigned  
Art Unit: 1645

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to MAIL STOP AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the 28<sup>th</sup> day of April, 2005.

  
Kristin J. Ketelhut

MAIL STOP AMENDMENT

Commissioner For Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

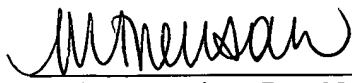
Transmitted herewith are the following documents:

- Information Disclosure Statement
- PTO Form 1449 with cited references
- Return Receipt Postcard

If the enclosed papers are considered incomplete, the Mail Room and/or the Application Branch is respectfully requested to contact the undersigned at (617) 646-8000, Boston, Massachusetts.

A check is not enclosed. If a fee is required, the Commissioner is hereby authorized to charge Deposit Account No. 23/2825. A duplicate of this sheet is enclosed.

Respectfully submitted,  
*Adams et al., Applicant*

By:   
Maria A. Trevisan, Reg. No.: 48,207  
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Docket No.: I0248.70024US00  
Date: April 28, 2005  
xNDDx



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Kristin J. Ketelhut

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**MAIL STOP AMENDMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

STATEMENT FILED PURSUANT TO THE DUTY OF  
DISCLOSURE UNDER 37 CFR §§1.56, 1.97 AND 1.98

Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, the Applicant requests consideration of this Information Disclosure Statement.

PART I: Compliance with 37 C.F.R. §1.97

This Information Disclosure Statement has been filed before the mailing date of a first Office Action on the merits in the above-identified case.

No fee or certification is required.

PART II: Information Cited

The Applicant hereby makes of record in the above-identified application the information listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

The Applicant hereby makes the following additional information of record in the above-identified application.

The above-identified U.S. application claims priority to application Serial No. PCT/US2003/021547. If the Examiner has not had the benefit of review of the file history of PCT/US2003/021547, then he/she is asked to contact the undersigned, who will provide a copy of same.

The Applicant would like to bring to the Examiner's attention the following co-pending applications that may contain subject matter related to this application:

<u>Docket No.</u>	<u>Serial No.</u>	<u>Filing Date</u>	<u>Inventor(s)</u>
I0248.70012US00	09/578,363	25 May 2000	Wallner et al.
I0248.70013US00	09/290,376	12 April 1999	Wallner
I0248.70014US00	09/744,658	13 August 1999	Wallner
I0248.70022WO00	PCT/US2005/00079	10 January 2005	McLean et al.
*I0254.70007US01	11/030,591	6 January 2005	Bachovchin
*I0254.70008US01	10/775,598	10 February 2004	Bachovchin
*I0254.70014US01	10/778,667	13 February 2004	Huber

\*a copy of this reference is not provided as the Office hereby waives the requirement under 37 CFR 1.98(a)(2)(iii) for submitting a copy of each cited U.S. patent application filed after June 30, 2003 and for applications filed before June 30, 2003, or that entered the national stage before June 30, 2003, if they are scanned to Image File Wrapper system and are available on Private PAIR.

### PART III: Remarks

Documents cited anywhere in the Information Disclosure Statement are enclosed unless otherwise indicated. It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited information has been fully considered by the Patent and Trademark Office during the examination of this application;
3. The citations for the information be printed on any patent which issues from this application.

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Conf. No.: 9289

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By submitting this Information Disclosure Statement, the Applicant makes no representation that a search has been performed, of the extent of any search performed, or that more relevant information does not exist.


By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. §1.56(b).

By submitting this Information Disclosure Statement, the Applicant makes no representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

Notwithstanding any statements by the Applicant, the Examiner is urged to form his own conclusion regarding the relevance of the cited information.

An early and favorable action is hereby requested.

Respectfully submitted,  
*Adams et al., Applicant*

By:   
\_\_\_\_\_  
Maria A. Trevisan, Reg. No. 48,207  
Wolf, Greenfield & Sacks, P.C.  
600 Atlantic Avenue  
Boston, Massachusetts 02210-2206  
Telephone: (617) 646-8000

Docket No.: I0248.70024US00  
Date: April 28, 2005  
xNDDx

FORM PTO-1449/A and B (Modified) <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		APPLICATION NO.: 10/616,409	ATTY. DOCKET NO.: I0248.70024US00
		FILING DATE: July 9, 2003	CONFIRMATION NO.: 9289
		APPLICANT: Adams et al.	
		GROUP ART UNIT: 1645	EXAMINER: Not Yet Assigned
Sheet	1	of	4

#### U.S. PATENT DOCUMENTS

Examiner's Initials	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication or of issue of Cited Document MM-DD-YYYY
		Number	Kind Code		
	A1	4,499,082		Shenvi et al.	02-12-1985
	A2	4,935,493		Bachovchin et al.	06-19-1990
	A3	5,288,707		Metternich	02-22-1994
	A4	5,296,604		Hanko et al.	03-22-1994
	A5	5,384,410		Kettner et al.	01-24-1995
	A6	5,444,049		de Nanteuil et al.	08-22-1995
	A7	5,462,928		Bachovchin et al.	10-31-1995
	A8	5,527,923		Klingler et al.	06-18-1996
	A9	5,543,396		Powers et al.	08-06-1996
	A10	5,587,299		Rettig et al.	12-24-1996
	A11	5,767,242		Zimmermann et al.	06-16-1998
	A12	5,965,373		Zimmermann et al.	10-12-1999
	A13	5,965,532		Bachovchin	10-12-1999
	A14	6,040,145		Huber et al.	03-21-2000
	A15	6,090,786		Augustyns et al.	07-18-2000
	A16	6,100,234		Huber et al.	08-08-2000
	A17	6,258,597	B1	Bachovchin et al.	07-10-2001
	A18	6,300,314	B1	Wallner et al.	10-09-2001
	A19	6,355,614	B1	Wallner	03-12-2002
	A20	6,503,882	B2	Huber et al.	01-07-2003
	A21	6,692,753	B2	Huber et al.	02-17-2004
	A22	6,703,238	B2	Bachovchin et al.	03-09-2004
	A23	6,770,628	B2	Wallner et al.	08-03-2004
	A24	6,825,169	B1	Bachovchin et al.	11-30-2004
	A25	6,846,910	B2	Zimmermann et al.	01-25-2005
	A26	6,875,737	B1	Bachovchin	04-05-2005
	A27	2003-0158114	A1	Wallner et al.	08-21-2003
	A28	2003-0212044	A1	Huber et al.	11-13-2003
	A29	2004-0077601	A1	Adams et al.	04-22-2004
	A30	2004-0152192	A1	Bachovchin et al.	08-05-2004
	A31	2005-0037976	A1	Wallner et al.	02-17-2005

#### FOREIGN PATENT DOCUMENTS

Examiner's Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/Country	Number	Kind Code			
	B1	EP	0 371 467	A2	Hoechst Aktiengesellschaft	06-06-1990	Y – Abst.
	B2	EP	0 615 978	A1	Adir et Compagnie	09-21-1994	Y – Abst.
	B3	EP	0 688 788	A1	Adir et Compagnie	06-22-1994	Y – Abst.

<b>FORM PTO-1449/A and B (Modified)</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>				APPLICATION NO.: 10/616,409		ATTY. DOCKET NO.: 10248.70024US00			
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Sheet	2	of	4						

Examiner's Initials	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document (not necessary)	Date of Publication of Cited Document MM-DD-YYYY	Translation (Y/N)
		Office/ Country	Number	Kind Code			
	B4	WO	89/03223	A1	Bachovchin et al.	04-20-1989	
	B5	WO	91/16339	A1	New England Medical Center Hospitals, Inc.	10-31-1991	
	B6	WO	91/17767	A1	New England Medical Center Hospitals, Inc.	11-28-1991	
	B7	WO	92/12140	A1	Georgia Tech Research Corporation	07-23-1992	
	B8	WO	93/08259	A2	New England Medical Center Hospitals, Inc.	04-29-1993	
	B9	WO	93/10127	A1	Boehringer Ingelheim Pharmaceuticals, Inc.	05-27-1993	
	B10	WO	93/16102	A1	Dana-Farber Cancer Institute	08-19-1993	
	B11	WO	94/03055	A1	The Government of the United States of America	02-17-1994	
	B12	WO	94/09132	A1	Dana-Farber Cancer Institute	04-28-1994	
	B13	WO	95/11689	A1	Trustees of Tufts College	05-04-1995	
	B14	WO	95/15309	A1	Ferring B.V.	06-08-1995	
	B15	WO	98/00439	A2	Trustees of Tufts College	01-08-1998	
	B16	WO	98/50046	A1	Trustees of Tufts College	11-12-1998	
	B17	WO	98/50066	A1	Trustees of Tufts College	11-12-1998	
	B18	WO	99/16864	A1	Point Therapeutics, Inc.	04-08-1999	
	B19	WO	99/56753	A1	Point Therapeutics, Inc.	11-11-1999	
	B20	WO	99/62914	A1	Point Therapeutics, Inc.	12-09-1999	
	B21	WO	00/10549	A1	Point Therapeutics, Inc.	03-02-2000	
	B22	WO	00/71135	A1	Point Therapeutics, Inc.	11-30-2000	
	B23	WO	2004/004658	A2	Point Therapeutics, Inc.	01-15-2004	
		WO	2004/004661	A2	Point Therapeutics, Inc.	01-15-2004	

#### OTHER ART — NON PATENT LITERATURE DOCUMENTS

Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)	
	C1	BAKER et al., Hydroxamates and aliphatic boronic acids: marker inhibitors for aminopeptidase. Biochemistry. 1983 Apr 26;22(9):2098-103.		
	C2	BORLOO et al., Dipeptidyl peptidase IV: development, design, synthesis and biological evaluation of inhibitors. Verh K Acad Geneesk Belg. 1994;56(1):57-88.		
	C3	HEGEN et al., The T cell triggering molecule Tp103 is associated with dipeptidyl aminopeptidase IV activity. J Immunol. 1990 Apr 15;144(8):2908-14. Abstract Only.		
	C4	JIANG et al., Inhibition of human immunodeficiency virus type 1 infection in a T-cell line (CEM) by new dipeptidyl-peptidase IV (CD26) inhibitors. Res Virol. 1997 Jul-Aug;148(4):255-66.		
	C5	KELLY et al., Immunosuppressive boronic acid dipeptides: correlation between conformation and activity. J Am Chem Soc. 1993;115:12637-8.		
	C6	KELLY et al., The efficient synthesis and simple resolution of a proline boronate ester suitable for enzyme inhibition studies. Tetrahedron. 1993;49:1009-16.		

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Examiner's Initials	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)	
	C7	KETTNER et al., Kinetic properties of the binding of alpha-lytic protease to peptide boronic acids. Biochemistry. 1988 Oct 4;27(20):7682-8.		
	C8	KETTNER et al., Peptide boronic acid inhibitors of trypsin-like proteases, their preparation and use as anticoagulants and inflammation inhibitors. Chemical Abstracts. 1990;112:80. Abstract number 91790c.		
	C9	KINDER et al., Antimetastatic activity of boro-amino acid analog protease inhibitors against B16BL6 melanoma in vivo. Invasion Metastasis. 1992;12(5-6):309-19.		
	C10	KINDER et al., Analogues of carbamyl aspartate as inhibitors of dihydroorotase: preparation of boronic acid transition-state analogues and a zinc chelator carbamylhomocysteine. J Med Chem. 1990 Feb;33(2):819-23.		
	C11	KINDER et al., Acylamino boronic acids and difluoroborane analogues of amino acids: potent inhibitors of chymotrypsin and elastase. J Med Chem. 1985 Dec;28(12):1917-25.		
	C12	KUBOTA et al., Involvement of dipeptidyl peptidase IV in an in vivo immune response. Clin Exp Immunol. 1992 Aug;89(2):192-7.		
	C13	KUBOTA et al., Dipeptidyl peptidase IV (DP IV) activity in serum and on lymphocytes of MRL/Mp-lpr/lpr mice correlates with disease onset. Clin Exp Immunol. 1994 May;96(2):292-6.		
	C14	REINHOLD et al., Inhibitors of dipeptidyl peptidase IV (DP IV, CD26) induces secretion of transforming growth factor-beta 1 (TGF-beta 1) in stimulated mouse splenocytes and thymocytes. Immunol Lett. 1997 Jun;58(1):29-35.		
	C15	SCANLAN et al., Molecular cloning of fibroblast activation protein alpha, a member of the serine protease family selectively expressed in stromal fibroblasts of epithelial cancers. Proc Natl Acad Sci U S A. 1994 Jun 7;91(12):5657-61.		
	C16	SCHARPE et al., Purified and cell-bound CD26: enzymatic inhibition, antibody binding profile, and expression on T cells in relation to other surface markers. Verh K Acad Geneesk Belg. 1994;56(6):537-59.		
	C17	SCHON et al., Dipeptidyl peptidase IV in the immune system. Effects of specific enzyme inhibitors on activity of dipeptidyl peptidase IV and proliferation of human lymphocytes. Biol Chem Hoppe Seyler. 1991 May;372(5):305-11.		
	C18	SCHON et al., The dipeptidyl peptidase IV, a membrane enzyme involved in the proliferation of T lymphocytes. Biomed Biochim Acta. 1985;44(2):K9-15. Abstract Only.		
	C19	SCHON et al., Dipeptidyl peptidase IV in human T lymphocytes. An approach to the role of a membrane peptidase in the immune system. Biomed Biochim Acta. 1986;45(11-12):1523-8. Abstract Only.		
	C20	SCHON et al., The role of dipeptidyl peptidase IV in human T lymphocyte activation. Inhibitors and antibodies against dipeptidyl peptidase IV suppress lymphocyte proliferation and immunoglobulin synthesis in vitro. Eur J Immunol. 1987 Dec;17(12):1821-6. Abstract Only.		
	C21	SNOW et al., Studies on Proline Boronic Acid Dipeptide Inhibitors of Dipeptidyl Peptidase IV: Identification of a Cyclic Species Containing a B-N Bond. J Am Chem Soc. 1994;116:10860-9.		
	C22	SUBRAMANYAM et al., Chapter 9: CD26, a T-cell accessory molecule induction of antigen-specific immune-sppression by inactivations of CD26: A clue to the AIDS paradox? in Dipeptidyl Peptidase IV (CD26) in Metabolism and Immune Response, edited by Bernhard Fleischer. 1995: R.G. Landes Company, p155-62.		
	C23	TANAKA et al., Cloning and functional expression of the T cell activation antigen CD26. J Immunol. 1992 Jul 15;149(2):481-6. Erratum in: J Immunol. 1993 Mar 1;150(5):2090.		
	C24	TANAKA et al., The costimulatory activity of the CD26 antigen requires dipeptidyl peptidase IV enzymatic activity. Proc Natl Acad Sci U S A. 1993 May 15;90(10):4586-90. Abstract Only.		
	C25	THOMPSON et al., Chapter 19: Peptide aldehydes: potent inhibitors of serine and cysteine proteases. in Methods in Enzymology, Volume 46. Colowick et al., eds. p220-5.		

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	C26	WELCH et al., Fluoroolefin containing dipeptide isosteres as inhibitors of dipeptidyl peptidase IV(CD26). Tetrahedron. 1996 January 1;52(1):291-304.		
	C27	WESLEY et al., A role for dipeptidyl peptidase IV in suppressing the malignant phenotype of melanocytic cells. J Exp Med. 1999 Aug 2;190(3):311-22.		
	C28	WOOD et al., Tetrapeptide inhibitors of the IgA1 proteinases from type I Neisseria gonorrhoeae. J Med Chem. 1989 Oct;32(10):2407-11.		
	C29	YOSHIMOTO et al., Comparison of inhibitory effects of prolinal-containing peptide derivatives on prolyl endopeptidases from bovine brain and Flavobacterium. J Biochem (Tokyo). 1985 Oct;98(4):975-9.		

EXAMINER:	DATE CONSIDERED:
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#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

\*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial No. \_\_, filed \_\_, and relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

[NOTE - The Office hereby waives the requirement under 37 CFR 1.98 (a)(2)(i) for submitting a copy of each cited U.S. patent and each U.S. patent application publication for all U.S. national patent applications filed after June 30, 2003 and for all international applications that have entered the national stage under 35 USC 371 after June 30, 2003. See 37 CFR 1.491(b). For all patent applications filed on or before June 30, 2003, copies of cited U.S. patents and patent application publications are still required unless an eIDS is filed. Copies of all other patent(s), publication(s), or other information listed must still be provided, even if it was previously submitted to, or cited by, the U.S. Patent Office in an earlier application, unless the earlier application is identified by the IDS and is relied upon for an earlier filing date under 35 U.S.C. §120, and the copy was provided in the earlier application.]